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Increase of bone and joint tuberculosis in The Netherlands

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There has been an increase in the incidence of bone and joint tuberculosis (BJTB) in The Netherlands and we have carried out an epidemiological study in order to find an explanation for this increase. Data from 1993 to 2000 from The Netherlands Tuberculosis Register (NTR) were used. In 1993 there was a total of 52 patients with BJTB. This figure increased gradually to 80 in 1999 before decreasing to 61 in 2000.

There was a total of 12 447 patients with tuberculosis; BJTB was found in 532, accounting for 4.3% of all cases and 10.6% of all extrapulmonary cases. Localisation in the spine occurred in 56%.

Certain immigrants, in particular from Somalia, were more likely to have BJTB than other immigrants or the native Dutch population. Increased age and female gender were associated with BJTB. Only 15% of BJTB patients also suffered from pulmonary tuberculosis. The usual long delay in the diagnosis of BJTB may be shortened if physicians are more aware of tuberculosis.

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There has been an increase in the incidence of bone and joint tuberculosis (BJTB) in The Netherlands during recent years. We have carried out an epidemiological study to find an explanation for this increase and now present a statistical analysis of demographic- and person- and illness-related factors.

Patients and Methods

All data were extracted from The Netherlands Tuberculosis Register (NTR) held by Royal Dutch Tuberculosis Foundation. This register contains data on patients with tuberculosis in The Netherlands from 1993; we have examined the figures from between 1993 and 2000. Every physician in The Netherlands is legally obliged to report a case of tuberculosis to the health authorities. In addition, anonymous data are reported by municipal health services to the NTR on a voluntary basis. Data include details of the patients, diagnosis, bacteriological findings (smear, culture), treatment regimens and outcome. All extrapulmonary tuberculosis is classified according to the site of the lesion, using the 9-International Classification of Diseases (ICD-9) classification. A successful outcome of treatment is defined as cure of the patient or completion of treatment.[1] Every immigrant from an endemic area for tuberculosis (incidence greater than 50 per 100 000) has a chest radiograph taken on arrival in The Netherlands. Voluntary screening is carried out every six months for the first two years.

Table I. Details of the site of origin of tuberculosis in Dutch and non-Dutch patients

	Dutch	Non-Dutch	Total
Spinal	105	203	308
Other BJTB	102	122	224
Other extrapulmonary	1604	2902	4506
Pulmonary	3504	3905	7409
Total	5315	7132	12 447

Results

The total number of patients with tuberculosis was 12 447 in the period studied. Pulmonary tuberculosis was present in 7409 (60%), and extrapulmonary tuberculosis in 5038 (40%) (Table I). Of the latter group, 1008 had both pulmonary and extrapulmonary tuberculosis. A total of 532 cases of BJTB was found (Table I), accounting for 4.3% of all cases and 10.6% of all extrapulmonary cases. Of the patients with BJTB, 163 (31%) also had extraskeletal lesions, 50% of which were pulmonary. This means that only 15% of BJTB patients had concurrent pulmonary tuberculosis.

In 1993 a total of 52 patients had BJTB. This figure increased gradually to 80 in 1999, then decreased to 61 in 2000 (Table II). Univariate analysis of the incidence of BJTB compared

Table II. Variables in BJTB *versus* all forms

Variables	BJTB	Total	Crude OR*	Adjusted OR* (95% CI)†	
Year			(p < 0.05)		
1993	52	1579	1		
1994	62	1798	1.05		
1995	74	1612	1.41		
1996	58	1657	1.07		
1997	75	1475	1.57		
1998	70	1358	1.60		
1999	80	1545	1.60		
2000	61	1423	1.32		
Gender			p < 0.001		
Male	261	7429	1	1	
Female	271	5018	1.57	1.53	(1.28 to 1.83)
Age group (yrs)			p < 0.001		
< 25	93	2989	1		
25 to 34	149	3372	1.44	1.53	(1.17 to 1.99)
35 to 44	72	1973	1.18	1.46	(1.06 to 2.01)
45 to 54	63	1150	1.80	2.55	(1.81 to 3.58)
55 to 64	43	891	1.58	2.42	(1.64 to 3.57)
65 to 74	52	909	1.89	2.85	(1.96 to 4.15)
75+	60	1163	1.69	2.58	(1.77 to 3.74)
Country of origin			p < 0.001		
Netherlands	207	5315	1	1	
Morocco	33	1224	0.68	0.87	(0.59 to 1.28)
Somalia	123	1572	2.09	3.11	(2.37 to 4.08)
Turkey	9	621	0.36	0.48	(0.24 to 0.95)
Other Africa	49	1070	1.18	1.85	(1.31 to 2.62)
Other Asia	70	1429	1.27	1.61	(1.20 to 2.17)
Not reported	41	1216	0.86	1.09	(0.76 to 1.55)

* odds ratio
† confidence interval

Table III. Variables associated with spinal tuberculosis *versus* all forms of BJTB

Variables	Spinal	All BJTB	Crude OR* (95% CI)	
Year			p > 0.2	
1993	29	52	1	
1994	32	62	0.85	
1995	43	74	1.10	
1996	33	58	1.05	
1997	50	75	1.59	
1998	38	70	0.94	
1999	50	80	1.32	
2000	33	61	0.93	
Gender			p > 0.2	
Male	156	261	1	
Female	152	271	0.86	
Age group (yrs)			p < 0.05	
< 25	49	93	1	
25 to 34	98	149	1.73	(1.02 to 2.93)
35 to 44	48	72	1.80	(0.95 to 3.40)
45 to 54	39	63	1.46	(0.76 to 2.80)
55 to 64	25	43	1.25	(0.60 to 2.59)
65 to 74	25	52	0.83	(0.42 to 1.64)
75+	24	60	0.60	(0.31 to 1.16)
Nationality			p > 0.05	
Netherlands	105	207	1	
Morocco	20	33	1.49	
Somalia	71	123	1.33	
Turkey	6	9	1.94	
Other Africa	34	49	2.20	
Other Asia	43	70	1.55	
Other or missing	29	41	2.35	

* odds ratio

with that of all tuberculosis has shown an increase in BJTB in recent years (Table II). The decrease in the year 2000 should be considered a statistical anomaly. The incidence of BJTB in Dutch and non-Dutch subjects is shown in Figure 1, indicating that the increase is restricted to non-Dutch subjects (r = 0.76; 95% confidence interval 0.11 to 0.95). In the native Dutch population there was no significant change in the incidence of BJTB during this period. The Netherlands have a population of 16 million of whom 2.5 million are immigrants. The largest immigrant groups in the year 2000 were from Surinam (280 000), Turkey (270 000), and Morocco (240 000). The incidence of tuberculosis increased from 8.2 in 1987 to 11.8 in 1994, but decreased to 8.9 in 2000. The incidence in 2000 was 3.4 per 100 000 for the Dutch and 136 per 100 000 for immigrants.

Of all patients with tuberculosis, 60% were men and 40% women. In the BJTB group there were 261 men and 271 women (49% *v* 51%); (Table II). Women were relatively more affected by BJTB (odds ratio (OR), 1.57). BJTB was associated with increasing age (Table II) and was more common among Somalians (OR, 2.09), and less common among Turks (OR, 0.36) and Moroccans (OR 0.68) (Table II).

The localisation of BJTB was spinal in 308 of the 532 patients (58%) and elsewhere in the skeleton in 224 (42%) (Table I). Compared with all BJTB there was a decrease in spinal tuberculosis with increasing age (Table III). Spinal tuberculosis was more common among non-Dutch than Dutch patients (Table I), but this difference was not significant if all nationalities were considered separately (Table III).

Delay in diagnosis by both patients and doctors is shown in Figure 2 for pulmonary, other and spinal tuberculosis. The mean delay for spinal tuberculosis was 29 weeks and for other BJTB, 35 weeks. The mean duration of treatment

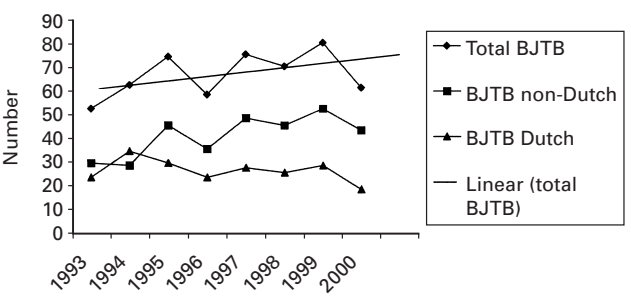

Fig. 1

Comparison of the incidence of BJTB between Dutch and non-Dutch populations from 1993 to 2000.

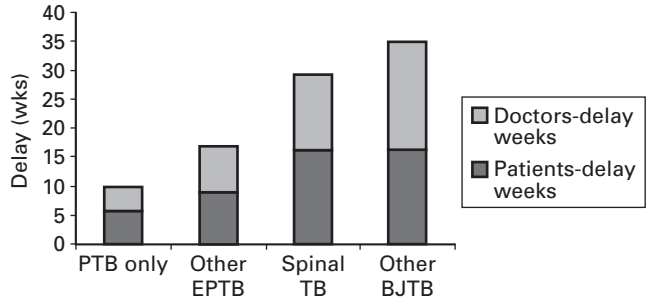

Fig. 2

Delay in diagnosis by patients and doctors for PTB, EPTB except BJTB, spinal TB and other BJTB (in weeks).

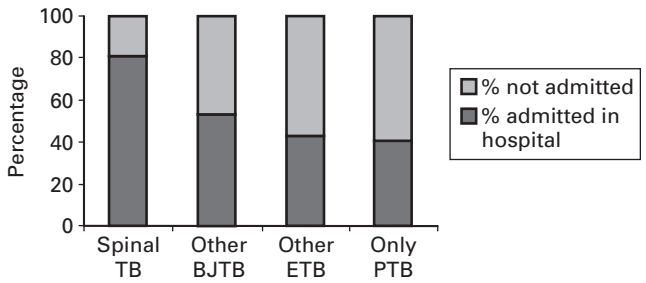

Fig. 3

Percentage of patients admitted and not admitted for the various forms of tuberculosis.

Table IV. Mean duration of treatment (days) and hospital admission (days) for the various forms of tuberculosis

	Duration of treatment	Duration of hospital admission
Spinal	340	24
Other BJTB	304	21
Other extrapulmonary	258	12
Pulmonary only	222	12

for the various forms of tuberculosis is shown in Table IV, 340 days for spinal and 304 days for other BJTB, compared with 222 days for pulmonary tuberculosis. The mean duration of hospital admission was 24 days for spinal tuberculosis, 21 days for other BJTB, and 12 days for pulmonary (Table IV). Patients were admitted to hospital in the following proportions: 41% of all pulmonary patients, 43% of other extrapulmonary tuberculosis, 53% of other BJTB, and 80% of spinal tuberculosis (Fig. 3). The outcome of treatment was generally good for all forms (Table V).

Discussion

An increase in the incidence of bone and joint tuberculosis was observed between 1993 and 2000. Ethnicity, age and female gender were associated with the disease. Only 15% of BJTB patients also suffered from pulmonary tuberculosis. We noted a significant delay by both patients and doctors between the first symptoms and the commencement of treatment. There is good evidence to show that tuberculosis is reported according to the guidelines of notifiable disease, from the close correlation between the actual use of pyrazinamide according to the Dutch Drug Information Project of the Health Care Insurance Board and the data registered with the NTR.[2] Cross-matching of notification data, data from laboratory surveillance and data in the NTR suggest a correlation of 95%. Van Nispen-Dobrescu (unpublished data) evaluated the between-person repeatability of completing the forms. She has shown that repeatability is moderate to good for the variables studied in this report.

Culture results are recorded in the NTR, but the origin of the material from which the cultures were taken was not stated, which means that some assumptions regarding the diagnosis have been made. The only proof for a skeletal lesion is a positive culture of material from the lesion, but even then only 47% to 81% of positive results can be expected.[3-5]

There was an increase in the incidence of BJTB from 52 to 80 patients per year between 1993 and 1999. According to statistical analysis, the decrease to 61 in the year 2000 is considered to be a statistical anomaly rather than a true drop which we expect to be confirmed by the figures for the years to come. Active pulmonary tuberculosis may be discovered at the obligatory first screening on arrival in the country. Vos et al[6] have shown that a decade after their arrival, the incidence of tuberculosis among immigrants is still high. Furthermore, a relatively larger percentage develop BJTB. In the native Dutch there was no significant change in the incidence during the period studied. The conclusion is that the increased incidence of BJTB is entirely attributable to immigration.

Table V. Treatment outcome from 1993 to 2000. The results are given for 4685 of 5038 (93%) patients with extrapulmonary tuberculosis and for 6844 of 7409 (92%) with pulmonary tuberculosis, by number and *percentage*

	Cured on treatment completed		Died		Defaulted or transferred out		Total
Spinal	271	*89*	17	*6*	18	*6*	306
Other BJTB	193	*86*	16	*7*	15	*7*	224
Other extrapulmonary	3452	*83*	302	*7*	401	*10*	4155
Pulmonary only	5661	*83*	523	*8*	660	*10*	6844

The fact that certain ethnic groups showed a preponderance towards BJTB is surprising, although other authors have reported similar findings.[3,5,7-9] In a large series from the USA,[10] neither ethnicity nor country of origin was associated with BJTB. Increasing age and female gender (adjusted OR, 1.7) did show an association similar to our findings.

The relatively younger age of the immigrants with BJTB probably reflects the changing general epidemiology of tuberculosis. However, BJTB occurs at a relatively older age if adjusted for nationality. Regarding age, several reports have described different age distributions for tuberculosis in whites and non-whites.[3,7,10-13] Possible explanations for this include a different distribution in age between various parts of the world, a younger exposure and the varying prevalence with age. From endemic regions it is well known that BJTB commonly involves young children.[13] This is in contrast to our findings. The different patterns of progression from infection to disease may also play a role, depending on ethnicity, former habitat and previous contact with the organism concerned.

The spine was the most common site of BJTB, which accords with the literature.[7,13] Spinal tuberculosis was more common among non-Dutch than Dutch patients in our study. Other authors have reported similar findings.[3,5]

It must be stressed that only 15% of BJTB patients in our series also suffered from pulmonary tuberculosis. Other authors have reported this incidence to be between 20% and 25%.[3,8] A normal chest radiograph does not of course rule out BJTB.

In our study, a lengthy delay by both patients and doctors was found for BJTB (mean period 32 weeks). In France, a mean delay of 12 weeks has been reported.[11,14] The explanation for the long medical delay in The Netherlands is probably a low index of suspicion and declining expertise.[1] In general, delay in diagnosis increases the risk of a fatal outcome. The long delay for BJTB in this population did not result in greater mortality but less delay must diminish morbidity.

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